

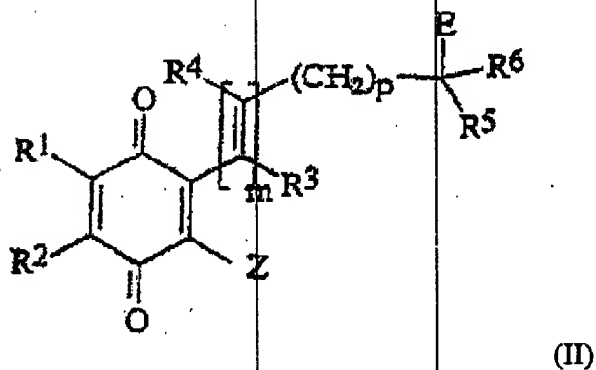
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January 15, 2009

**AMENDMENTS TO THE CLAIMS:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

1-5 (Cancelled).

6. (Currently Amended) A bio-reductive conjugate ~~as claimed in claim 1~~ of the formula II:



(wherein

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$R^1$  and  $R^2$  independently represent hydrogen or halogen atoms, or a group R, OR, SR, NHR,  $NR_2$ ,  $CO_2R$  or CONHR;

or, alternatively,  $R^1$  and  $R^2$  together with the intervening ring carbon atoms form a 5-7 membered carbocyclic or heterocyclic ring itself optionally substituted by one or more halogen atoms, or by one or more groups selected from R, OR, SR, NHR,  $NR_2$ ,  $CO_2R$  and CONHR;

Z represents an alkyl, alkenyl, aryl or aralkyl group optionally carrying at least one OH, SH,  $NH_2$  or  $NHR^7$  group in which  $R^7$  is an alkyl group or Z represents a group of the formula  $-XH$  where X represents an oxygen or a sulphur atom, or a group of formula NY in which Y represents a hydrogen atom or an alkyl group;

$R^3$ ,  $R^4$ ,  $R^5$  and  $R^6$  independently represent hydrogen atoms or an alkyl or alkenyl group;

each group R independently represents a hydrogen atom, an alkyl or alkenyl group;

E represents the residue of a therapeutic agent to be delivered, optionally attached via a linking group L which is an ester, phosphate ester, ether, amine, thiol or thiol ester group or any combination thereof;

$m = 0, 1, 2$  or  $3$ ; and

$p = 0$  or  $2$ ;

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with the proviso that when  $m = 1$  then  $p = 0$ )

or a salt thereof.

7. (Previously Presented) A bioreductive conjugate as claimed in claim 6, wherein in formula II:

Z represents a group of the formula  $(CH_2)_nXH$ ;

$n = 1, 2$  or  $3$ ;

X represents an oxygen or sulphur atom, or a group of formula NY in which Y represents a hydrogen atom or an alkyl group;

or a salt thereof.

8. (Previously Presented) A bioreductive conjugate as claimed in claim 6, wherein in formula II:

Z represents a group of the formula XH in which X represents an amino group;

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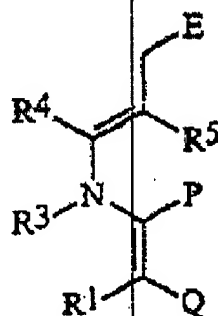
$R^1$  and  $R^2$  each represent alkoxy groups or, together with the intervening ring carbon atoms,  $R^1$  and  $R^2$  form a benzene ring;

$R^3$ ,  $R^4$ ,  $R^5$  and  $R^6$  each represent hydrogen atoms; and

$n = m = 1$  and  $p = 0$ ;

or a salt thereof.

9. (Currently Amended) A bioreductive conjugate as claimed in claim 1 of formula III:



(III)

(wherein

P and Q together with the intervening ring carbon atoms form a quinone or indoloquinone ring, an ~~a nitroaromatic~~, N-oxide or diazoaromatic compound, itself optionally substituted by one or more halogen atoms, or by one or more groups selected from R, OR, SR, NHR,  $NR_2$ ,  $CO_2R$  and CONHR;

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$R^1$  represents a hydrogen or halogen atom, or a group R,  
OR, SR, NHR,  $NR_2$ ,  $CO_2R$  or CONHR;

$R^3$ ,  $R^4$  and  $R^5$  independently represent hydrogen atoms or an alkyl or alkenyl group;

each group R independently represents a hydrogen atom, an alkyl or alkenyl group; and

E represents the residue of a therapeutic agent to be delivered, optionally attached via a linking group L which is an ester, phosphate ester, ether, amine, thiol or thiol ester group or any combination thereof;

or a salt thereof.

10. (Original) A bioreductive conjugate as claimed in claim 9, wherein in formula III;

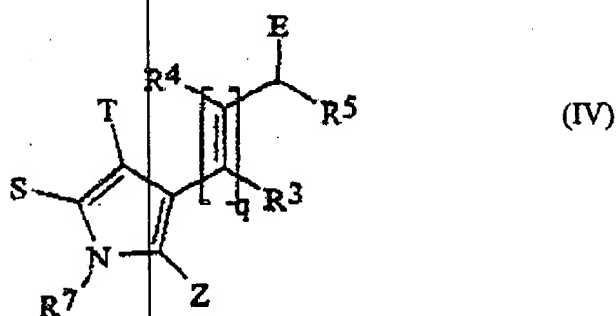
P and Q together with the intervening ring carbon atoms form a quinone or indoloquinone ring;  
and

$R^1$ ,  $R^3$ ,  $R^4$  and  $R^5$  each represent hydrogen atoms or methyl groups;

or a salt thereof.

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11. (Currently Amended) A bioreductive conjugate ~~as claimed in claim 1~~ of formula IV:



(wherein

S and T together with the intervening ring carbon atoms form a quinone or iminoquinone indoloquinone ring, ~~an aromatic or N-oxide compound~~, itself optionally substituted by one or more halogen atoms, or by one or more groups selected from R, OR, SR, NHR, NR<sub>2</sub>, CO<sub>2</sub>R and CONHR;

Z represents an alkyl, alkenyl, aryl or aralkyl group optionally carrying at least one OH, SH, NH<sub>2</sub> or NHR<sup>6</sup> group in which R<sup>6</sup> is an alkyl group;

R<sup>7</sup> represents an alkyl group;

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$R^3$ ,  $R^4$  and  $R^5$  independently represent hydrogen atoms or an alkyl or alkenyl group;

each group R independently represents a hydrogen atom, an alkyl or alkenyl group;

$q = 0, 1, 2$  or  $3$ ; and

E represents the residue of a therapeutic agent to be delivered, optionally attached via a linking group L which is an ester, phosphate ester, ether, amine, thiol or thiol ester group or any combination thereof;

or a salt thereof.

12. (Original) A bioreductive conjugate as claimed in claim 11, wherein in formula IV:

S and T together with the intervening ring carbon atoms form a quinone or N-oxide compound;

$R^3$ ,  $R^4$  and  $R^5$  each represent hydrogen atoms;

$R^7$  is methyl;

Z represents a group of formula  $(CH_2)_nXH$  wherein X represents an oxygen or sulphur atom, or

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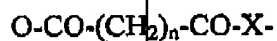
X represents a group of formula NY in which Y represents a hydrogen atom or an alkyl group;  
and

q = 0 or 1,

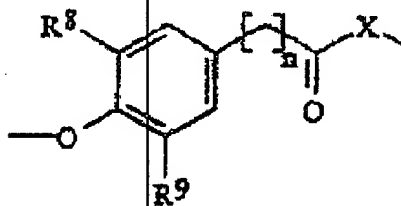
or a salt thereof.

13-16 (Cancelled).

17. (Currently Amended) A bio-reductive conjugate as claimed in claim ~~15~~ 6 wherein  
said linker group L if present is a group of the formula:



or



(wherein n is an integer from 1 to 3;



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X represents a sulphur or oxygen atom; and

R<sup>8</sup> and R<sup>9</sup> each independently represent F or Cl).

18 and 19 (Cancelled).

20. (Currently Amended) A pharmaceutical composition comprising a bioreductive conjugate as claimed in claim 4 6, or a pharmaceutically acceptable salt thereof, together with at least one pharmaceutical carrier or excipient.

21. (Currently Amended) A bioreductive conjugate as claimed in claim 4 6 for use in a method of targeting a therapeutic agent to a site of hypoxia and/or ischemia within the human or non-human animal body.

22. (Currently Amended) A bioreductive conjugate as claimed in claim 4 6 for use in the treatment of rheumatoid arthritis or other arthritic conditions, diabetes, atherosclerosis, stroke, sepsis, Alzheimer's disease and other neurological disorders, cancer, kidney disease, digestive diseases, liver disease, chronic periodontitis or ischemia following tissue transplantation.

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23. (Currently Amended) Use of a bioreductive conjugate as claimed in claim 4 6 in the manufacture of a medicament for use as a targeting agent capable of targeting a site of hypoxia and/or ischemia within the human or non-human animal body.

24. (Original) Use as claimed in claim 22 for the treatment of rheumatoid arthritis or other arthritic conditions, diabetes, atherosclerosis, stroke, sepsis, Alzheimer's disease and other neurological disorders, cancer, kidney disease, digestive diseases, liver disease, chronic periodontitis or ischemia following tissue transplantation.

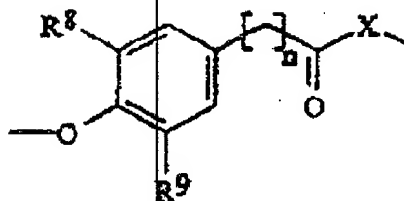
25. (Currently Amended) A method of targeting hypoxic and/or ischemic tissues in the human or non-human animal body, said method comprising administering to said body a bioreductive conjugate as claimed in claim 4 6.

26. (New) A bioreductive conjugate as claimed in claim 9 wherein said linker group L if present is a group of the formula:



or

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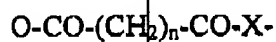


(wherein n is an integer from 1 to 3;

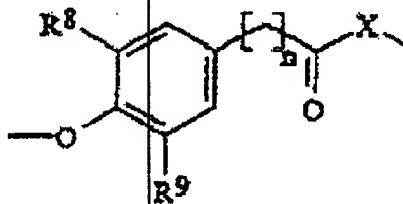
X represents a sulphur or oxygen atom; and

R<sup>8</sup> and R<sup>9</sup> each independently represent F or Cl).

27. (New) A bioreductive conjugate as claimed in claim 11 wherein said linker group L if present is a group of the formula:



or



(wherein n is an integer from 1 to 3;

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X represents a sulphur or oxygen atom; and

R<sup>8</sup> and R<sup>9</sup> each independently represent F or Cl).

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